Characteristics of adult MASH patients and factors associated with MASH-relevant clinical endpoints in a real-world US cohort

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Background

- Metabolic dysfunction associated steatohepatitis (MASH) affects 3-5% of adults in the United States[1]
- Approximately 20% of all MASH patients suffer from advanced fibrosis, which can lead to end-stage liver disease, hepatocellular carcinoma, liver transplantation and death[2-3]

Objectives:

- To describe characteristics of patients with MASH by disease severity, and to investigate factors associated with MASH-relevant clinical endpoints in routine clinical practice

Methods

Study Design & Data Source

- A retrospective cohort study was conducted using the TARGET-NASH database- a real-world longitudinal observational cohort following >6000 patients enrolled across academic and community sites in the US
- Patients are enrolled at a participating center in TARGET-NASH upon a diagnosis of MASLD by a treating physician in routine care
- Data used was from 08/01/2016 through 01/26/2024 (study period)
- Baseline demographics and clinical characteristics were assessed in the 36 months prior to the index date (defined as the date of enrollment in TARGET-NASH)
- Patients were grouped into three subgroups for this study:
  - MASH without cirrhosis (MASH)
  - MASH with compensated cirrhosis (CC)
  - MASH with decompensated cirrhosis (DCC)

Statistical Analysis:

- Descriptive statistics were used to summarize cohort characteristics
- Fine-Gray[4] multivariable hazard models, adjusted for competing risks were used to assess the longitudinal risk of composite clinical endpoints following enrollment by disease type. Model covariates (Figures 1-3) were selected based on their relevance to the research context and statistical significance from the univariate modeling

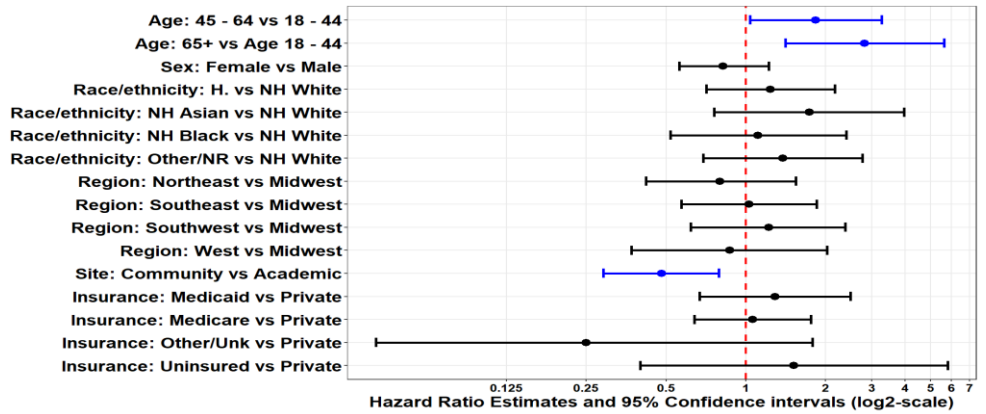
Results

Table 1. Patient Demographics at Enrollment

	MASH (n=1084)	Compensated Cirrhosis (n=495)	Decompensated Cirrhosis (n=370)
Median Age (years)	55	62	63
Female, n(%)	689 (64)	297 (60)	205 (55)
Non-Hispanic White, n(%)	720 (66)	387 (78)	303 (82)
Academic Setting, n(%)	688 (64)	387 (78)	304 (82)
Private Insurance, n(%)	717 (66)	250 (51)	145 (39)
FIB-4 category[1], n(%)			
Low	588 (66)	82 (19)	14 (4)
Indeterminate	254 (28)	132 (30)	60 (17)
High	56 (6)	227 (52)	290 (80)
Hypertension, n(%)	659 (61)	397 (80)	352 (95)
Type 2 Diabetes, n(%)	496 (46)	321 (65)	266 (72)
Obesity, n(%)	698 (64)	357 (72)	269 (73)
CYP3A Inhibitors, n(%)	106 (10)	67 (14)	66 (18)

[1]FIB-4 categories are as follows: low risk (FIB-4 <1.3), indeterminate risk (FIB-4 >1.3 and <2.67), and high risk (FIB-4 >2.67).
Note: All measures were taken at or close to enrollment (index)

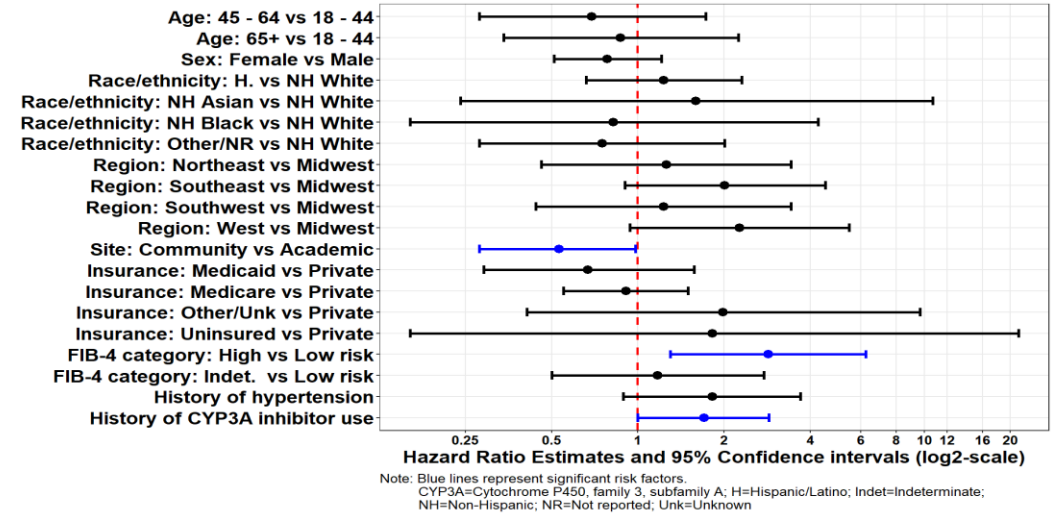
Figure 1. Hazard model in MASH patients without cirrhosis for the composite endpoint*



Note: Blue lines represent significant risk factors.
H=Hispanic/Latino; NH=Non-Hispanic; NR=Not reported; Unk=Unknown

* For patients with MASH without cirrhosis, the composite endpoint includes the following: progression to cirrhosis, change in MELD score from <12 to >15, FIB-4 change to >2.67 (advanced fibrosis) after enrollment date from FIB-4 <2.67 prior to enrollment, HCC, liver transplant, and all-cause mortality

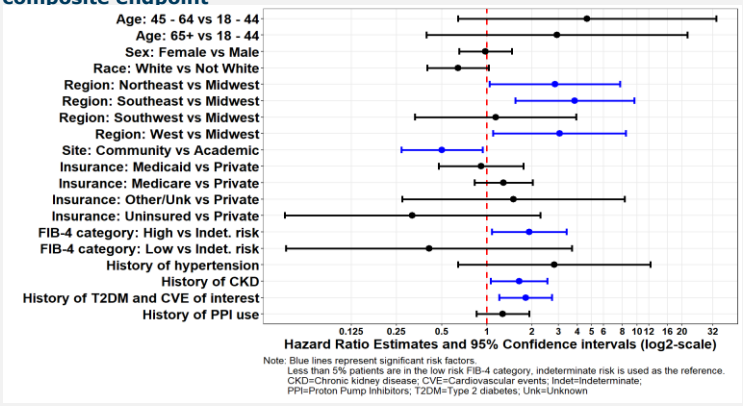
Figure 2. Hazard model in patients with compensated cirrhosis for the composite endpoint*



Note: Blue lines represent significant risk factors.
CYP3A=Cytochrome P450, family 3, subfamily A; H=Hispanic/Latino; Indet=Indeterminate; NH=Non-Hispanic; NR=Not reported; Unk=Unknown

* For patients with CC, the composite endpoint includes the following: any decompensation event (ascites and complications from ascites, variceal hemorrhage, hepatic encephalopathy), MELD score change to >15 after enrollment from MELD <12 prior to or at enrollment, HCC, liver transplant and all-cause mortality

Figure 3. Hazard model in decompensated cirrhosis patients for the composite endpoint*



Note: Blue lines represent significant risk factors.
Less than 5% patients are in the low risk FIB-4 category, indeterminate risk is used as the reference.
CKD=Chronic kidney disease; CVE=Cardiovascular events; Indet=Indeterminate;
PPI=Proton Pump Inhibitors; T2DM=Type 2 diabetes; Unk=Unknown

* For patients with DCC, the composite endpoint includes the following: HCC, liver transplant, and all-cause mortality

Results (cont.)

- Among patients with MASH, increasing age (45-64 - HR 1.84, 95% CI 1.04, 3.26, p=0.04; 65+ - HR 2.81, 95% CI 1.41, 5.61, p=0.003) was associated with an increased risk of experiencing a composite endpoint; treatment at community sites was associated with decreased risk of experiencing a composite endpoint
- Among patients with CC, patients receiving care at a community site were less likely to progress (HR 0.53, 95% CI 0.28, 0.98, p=0.04), while those with a high-risk FIB-4 category (HR 2.85, 95% CI 1.30, 6.24, p=0.009) and a history of CYP3A inhibitor use (HR 1.70, 95% CI 1.00, 2.87, p=0.05) were more likely to progress to a cirrhosis composite endpoint
- For patients with DCC, patients receiving care in the Northeast (HR 2.84, 95% CI 1.05, 7.70, p=0.04), Southeast (HR 3.85, 95% CI 1.55, 9.58, 0.004), and West (HR 3.05, 95% CI 1.10, 8.45, p=0.03), with a high risk FIB-4 category (HR 1.91, 95% CI 1.08, 3.39, p=0.027), history of both Type 2 Diabetes and cardiovascular events of interest (HR 1.81, 95% CI 1.21, 2.71, p=0.004) were more likely to progress to a composite endpoint. Similar to patients with non-cirrhotic MASH and CC, DCC patients receiving care at community sites (HR 0.50, 95% CI 0.27, 0.94, p=0.03) were less likely to progress to a composite endpoint

Limitations: Real-world databases are subject to potential missingness, limited generalizability and surveillance bias.

Conclusions

- A high overall burden of disease was shown among those with MASH, compensated cirrhosis and decompensated cirrhosis
- Receipt of care at an academic site (vs. community) was significantly associated with a higher risk of MASH-relevant clinical endpoints for all three cohorts, which may be due in part to patients with more complex conditions seeking care at these facilities
- For patients with more advanced disease, FIB-4 was significantly associated with MASH-relevant clinical endpoints

References: [1]Povsic M, et al. *A structure literature review of the epidemiology and disease burden of non-alcoholic steatohepatitis (NASH). Advances in therapy, 36, p. 1574-1594.* [2]Ekstedt MP, Nasr P, Kechagias S. *Natural history of NAFLD/NASH. Current hepatology reports, 2017. 16: p. 391-397.* [3]David K, et al. *Quality of life in adults with nonalcoholic fatty liver disease: baseline data from the nonalcoholic steatohepatitis clinical research network.* Hepatology, 2009. 49(6): p. 1904-1912. [4] Fine, J. P., & Gray, R. J. (1999). A Proportional Hazards Model for the Subdistribution of a Competing Risk. *Journal of the American Statistical Association*, *94*(446), 496–509.

Acknowledgements and Disclosures: Target RWE communities are collaborations among academic & community investigators, the pharmaceutical industry and patient community advocates. Target RWE communities are sponsored by TARGET PharmaSolutions Inc (d.b.a., Target RWE). The authors would like to thank all the investigators, participants, and research staff associated with TARGET-NASH. ClinicalTrials.gov Identifier: NCT02815891. TK, MM, XZ, MC and GF are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, and may own stock and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA. This project was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA